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Mitochondrial fusion and fission proteins as novel therapeutic targets for treating cardiovascular disease

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ABSTRACT

The past decade has witnessed a number of exciting developments in the field of mitochondrial dynamics – a phenomenon in which changes in mitochondrial shape and movement impact on cellular physiology and pathology. By undergoing fusion and fission, mitochondria are able to change their morphology between elongated interconnected networks and discrete fragmented structures, respectively. The cardiac mitochondria, in particular, have garnered much interest due to their unique spatial arrangement in the adult cardiomyocyte, and the multiple roles they play in cell death and survival. In this article, we review the role of the mitochondrial fusion and fission proteins as novel therapeutic targets for treating cardiovascular disease.

1. Introduction

In the heart, the mitochondria occupy nearly one third the volume of a cardiomyocyte – they sustain the energy required for normal cardiac contractile function by producing up to 30 kg of adenosine triphosphate (ATP) per day. However, the role of cardiac mitochondria extends far beyond that of being merely the 'powerhouse' of the cell. The past decade has witnessed a number of developments in the field of mitochondrial dynamics – a phenomenon in which changes in mitochondrial shape and movement have been demonstrated to impact on cellular physiology and pathology. Mitochondria are dynamic organelles which are able to change their shape by undergoing fusion to generate elongated interconnected mitochondrial networks, and fission to produce discrete fragmented mitochondria. These processes are under the regulation of the mitochondrial fusion and fission proteins, respectively, and are essential for maintaining a healthy mitochondrial network. The cardiac mitochondria, in particular, have garnered much interest due to their unique spatial arrangement in the adult heart, and the multiple roles they play in cell death and survival. It is known that the actions of the mitochondrial fusion and fission proteins extend beyond those of mediating changes in mitochondrial shape – in this regard these pleiotropic roles may impact on their effects in the heart and the vasculature (see Fig. 1). In this article, we review the potential role for the mitochondrial fusion and fission proteins as novel targets for treating cardiovascular disease.

2. Mitochondrial fusion

The fusion of two adjacent mitochondria allows the mixing of intra-mitochondrial proteins and the replacement of damaged

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